Remarks

Claims 28, 29, and 49 were pending in the subject application. By this Amendment, claims 28 and 49 have been amended and new claims 52-61 have been added. The undersigned avers that no new matter is introduced by this amendment. Support for the amendments and the new claims can be found throughout the specification including, for example, page 38 lines 14-16 (claims 28 and 49); page 14 lines 2-4 (claim 52); page 5 lines 24-28, page 14 lines 21-33, page 30 lines 10-31, page 42 line 29 through page 43 line 21, page 44 lines 20-30, and page 54 lines 7-19 (claim 53); page 29 lines 12-15 (claims 54 and 55); page 14 lines 9-13 and page 27 line 33 to page 28 line 2 (claim 56); page 30 line 32 to page 31 line 5 and page 38 lines 9-28 (claims 57 and 58); page 14 lines 17-18 and page 34 lines 20-24 (claim 59); and page 31 lines 7-13, page 52 lines 21-26, and page 53 lines 9-11 (claims 60 and 61). It should be understood that the amendments to the claims have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of the applicants' agreement with, or acquiescence in, the rejections of record.

Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 28, 29, 49 and 52-61 are currently before the Examiner for his consideration. Favorable consideration of the pending claims is respectfully requested.

The claims currently pending in the subject application are drawn to the applicants' unique system for specifically binding target double stranded polynucleotides. The claims have been amended herein to more clearly delineate the mechanism by which the subject invention achieves its advantageous specificity. The Target Binding Assemblies (TBAs) of the subject invention are made up of multiple nucleic acid recognition units each of which binds to discrete target sequences. The multiple nucleic acid recognition sites are directed to discrete sequences on a target double stranded polynucleotide molecule. When all of the multiple nucleic acid recognition sites bind to their corresponding target sequences, the combined effect is that the entire TBA (with its multiple nucleic acid recognition units) binds with great affinity and specificity to the target double stranded polynucleotide. In view of the unique structural and functional characteristics of the applicants' system, as reflected by the current claims, the applicants respectfully request favorable consideration of the claims now pending.

The applicants wish to thank Primary Examiner Ardin H. Marschel for the courtesy extended to the undersigned and his colleagues during the personal Examiner Interview conducted May 20, 2002. This amendment and response are submitted in accordance with the substance of that interview.

As an initial matter, the subject specification remains objected to because of informalities. Attached with this amendment are new formal drawings in which the use of lower case letters corresponds to the descriptions provided in the specification. No new matter has been added by these amendments. Reconsideration and withdrawal of the objection is respectfully requested.

The applicants gratefully acknowledge the Examiner's withdrawal of the rejections under 35 USC §112, first and second paragraphs. Further, the applicants appreciate the indication that claim 29 contains allowable subject matter. The applicants respectfully submit, as discussed below, that claim 28 (from which claim 29 depends) is now allowable in view of the amendments set forth herein.

Claim 28 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Frankel *et al.* (U.S. Patent No. 5,674,980). The applicants respectfully traverse this grounds for rejection because the Frankel *et al.* reference does not disclose or suggest the applicants' unique and advantageous method. Please note that, in order to eliminate any ambiguity which may have previously existed in claim 28, the applicants have amended that claim herein. In its amended form, it is clear from claim 28 that the applicants' method utilizes a combination of nucleic acid recognition units to facilitate a highly selective targeting process. Specifically, each nucleic acid recognition unit binds a specific target sequence of double stranded nucleic acid. Only when these multiple target sequences are present on a molecule will the TBA bind to that target molecule.

Thus, as set forth in the claims, the selectivity of TBAs of the subject invention is attributable to the TBAs having multiple binding units that act cooperatively. Each of these binding units is selective for an individual sequence within the target molecule. The entire TBA binds with great selectivity as the individual TBA binding units are cooperatively bound together.

The system of the subject invention is particularly unique and advantageous because the TBA binds selectively to a target double stranded polynucleotide, and discriminates for this target

compared to a different (non-target) molecule, even if the different (non-target) molecule contains sequences within it which are identical to sequences in the target molecule.

The Frankel *et al.* reference describes a system that uses molecules that are structurally distinct from the molecules used in the method of the present invention. Furthermore, as discussed below, the Frankel *et al.* system achieves a different purpose through a different mode of action. Specifically, the purpose of the Frankel *et al.* system is to transport cargo molecules into a cell. To achieve this transportation, Frankel *et al.* use the HIV tat protein (or portions thereof) to gain entry to a cell. The current applicants' system has nothing to do with using the tat protein to gain entry to a cell. Additionally, unlike the subject matter claimed by the current applicants, the Frankel *et al.* complexes do not have multiple nucleic acid recognition units that bind to distinct sites on a target double stranded DNA molecule.

Furthermore, because the Frankel *et al.* system is designed for a purpose that is quite different from the current applicants' purpose, there would be no motivation for a person skilled in the art to modify the Frankel *et al.* system to arrive at the current applicants' unique and advantageous method.

It has been well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield applicant's invention it would not have made the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125,1127 (Fed. Cir. 1984). However, as expressed by the CAFC, to support a §103 rejection, "[b]oth the suggestion and the expectation of success must be founded in the prior art ..." *In re Dow Chemical Co.* 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988). One finds neither the suggestion nor the expectation of success in the cited reference. An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using the applicants' disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56CCPA 823, 160 USPQ 237, 243 (1969). Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 based on the Frankel *et al.* reference.

Claim 49 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Essigmann *et al.* (U.S. Patent No. 5,882,941). The applicants respectfully traverse these grounds for rejection

because the cited reference does not disclose or suggest the claimed invention. Please note that claim 49 has been amended herein to add greater clarity to the claimed subject matter.

The outstanding Office Action indicates that this rejection has been maintained "because the open claim language term 'comprising' is present in claim 49 regarding the content of TBA(s) thus being inclusive of other entities as in Essigmann *et al.*" The applicants wish to emphasize, however, that it is not the presence in the Essigmann *et al.* molecule of the additional component which is important; rather, it is the absence of multiple nucleic acid recognition units in the Essigmann *et al.* molecule which is critical. It is the applicants' use of multiple nucleic acid recognition units which makes the current invention unique and advantageous. Such a use of multiple nucleic acid recognition units is not disclosed or suggested by Essigmann.

Essigmann *et al.* describe using heterobifunctional compounds where the first agent binds to cellular DNA to form a genomic lesion and the second agent is used to block DNA repair of the lesion caused by the first agent. Thus, the "second agent" of Essigmann *et al.* is not a nucleic acid recognition unit as required by the applicants' claims. Furthermore, there would be no reason for one skilled in the art to modify the Essigmann *et al.* teachings to arrive at the subject invention since the purpose of the "second agent" as described by Essigmann *et al.* is to "protect" the DNA lesion caused by the "first agent." Furthermore, nothing in the Essigmann *et al.* reference teaches or suggests the advantageous selectivity achieved using the system of the subject invention. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection of claim 49 under 35 U.S.C. §103.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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Attachment: Marked-Up Version of Amended Claims
Petition and Fee for Extension of Time

Docket No. GP-100C1
Serial No. 08/860,844

Marked-Up Version of Amended Claims

Claim 28 (four times amended):

A method of using a target binding assembly (TBA) wherein said TBA comprises a plurality of nucleic acid recognitions units wherein each of said nucleic acid recognition units binds to a specific nucleic acid sequence on a target double stranded nucleic acid molecule[, and optionally one or all of the sequences selected from the group consisting of a linker sequence, an assembly sequence, an asymmetry sequence, and a nuclear localization signal sequence (NLS)]; and wherein the combined binding affinity of said plurality of nucleic acid recognition units is such that said TBA specifically binds to the [a] target double stranded nucleic acid molecule [sequence] but does not bind to non-target molecules [sequences]; and wherein said method comprises administering to a patient a therapeutically or prophylactically effective amount of said TBA, or nucleic acid which codes for and produces said TBA, such that the TBA binds a target double stranded nucleic acid molecule [sequence] to achieve a desired prophylactic or therapeutic result.

Claim 49 (amended):

A method of assembling a multimeric target binding assembly (TBA) [assemblies (TBAs)] *in vivo* or *in situ* which comprises introducing components of said multimeric TBA, or nucleic acid which codes for and produces said TBA components, [TBAs] into a cell, said components each comprising a nucleic acid recognition unit[, and optionally comprising assembly sequences, asymmetry sequences, nuclear localization signal sequences, and linker sequences,] such that upon proximal binding via the nucleic acid recognition unit of each component to a specific nucleic acid sequence [sequences encountered in the nucleus or elsewhere in the cell], the components assemble into a multimeric TBA [TBAs]; wherein the combined binding affinity of said components is such that said assembled multimeric TBA specifically binds to a target double stranded nucleic acid [sequence] molecule but does not bind to non-target [sequences] molecules.